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ACUTE OTITIS MEDIA APEDIATRIC AND MICROBIAL CHALLENGE

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ABSTRACT

Acute otitis media (AOM) the most common bacterial infection in children worldwide. Common pathogens are mainly *Streptococcus pneumoniae*, *Haemophilis influenza*, *Moraxxella catarrahalis* and the respiratory viruses. Race and ethnicity provide additional data suggesting a genetic basis for recurrent middle ear infections. An increased incidence of AOM occurs in children with Down syndrome and in children with acquired immunodeficiency syndrome. Amoxicillin in high dose is the drug of choice in AOM, but ineffective in beta-lactamase producing pathogens. Alternatives to amoxicillin include amoxicillin-clavulanate and cephalosporin. Some children with AOM caused by bacterial pathogens improve without the use of antimicrobial agents. In one study showed that antibiotic treatment did not improve the rate of recovery of patients.

KEYWORDS: Acute Otitis Media, Children, *Streptococcus pneumoniae* and Antimicrobial Agents

INTRODUCTION

Acute Otitis Media (AOM) is defined as an acute illness marked by the presence of middle ear fluid and inflammation of the mucosa that lines the middle ear space. Otitis media with effusion (OME) is defined by the presence of middle ear without acute signs of or inflammation of middle ear mucosa. It usually follows AOM but may also occur as a result of barotrauma or allergy [1]. Children by the age of 3 years more than two third have had one or more episodes of AOM and one third have had three or more episodes [2]. The highest incidence of otitis media occurs between 6 months to 24 months of age. Otitis media is infrequent in adults, but the bacteriology and therapy are similar to those to children [3]. The vast majority of children have no obvious defect responsible for severe and recurrent otitis media, but small number have anatomic changes (cleft palate, cleft uvula, sub mucous cleft) alteration of normal physiological defenses (patulous Eustachian tube), or congenital or acquired immunologic deficiencies.

An increased incidence of AOM occurs in children with Down syndrome [4]. Children with acquired immunodeficiency syndrome have higher age-specific incidence of otitis media, beginning at 6 months of age, than uninfected children or children who initially were positive for human immunodeficiency virus antibody but who seroreverted [5]. Breast feeding for 3 or more months is associated with a decreased risk of AOM in the first year of life. Race and ethnicity provide additional data suggesting a genetic basis for recurrent middle ear infections; Native Americans, Alaskan and Canadian Eskimos and Australian aborigines have an extraordinary incidence and severity of OM [6] Young Australian Indigenous children in remote Northern Territory communities suffer excessively high rates of OM and remain at high risk of suppurative complications with poor audio logical and educational squeals [7].

In Australia, non-indigenous children frequently experience OME and occasionally suffer AOM. Perforation of tympanic membrane and suppurative complications are uncommon [8]. Signs and symptoms may be specific such as ear pain, ear drainage, or hearing loss, or nonspecific, such as fever, lethargy, or irritability. The microbiology of otitis media

has been demonstrated by appropriate culture of middle ear effusions obtained by needle aspiration. Pathogens are mainly: *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis* and others [9]. OM with *Mycobacterium tuberculosis* has been reported [10]. Early therapeutic intervention is important to minimizing the risk of children progressing into chronic suppurative otitis media (CSOM), if left untreated. The paper reviews the pathogenesis, management and therapy of AOM.

PATHOGENESIS

The middle ear is part of a continuous system that includes the nares nasopharynx, and eustachian tube medially and anteriorly and mastoid air cells posteriorly. Anatomic and physiologic dysfunction of eustachian tube appears to play a critical role in the development of otitis mediaeustachian has at least three physiologic functions with respect to the middle ear: protection of ear from nasopharyngeal secretions drainage into the nasopharynx of secretions produced within the middle ear, and ventilation of the middle ear to equilibrate air pressure with that in external ear canal. When one or more of these functions is compromised, the results may be the development of fluid and infection in the middle ear.

Most episodes of AOM occur in the following sequence: congestion of the mucosa of the upper respiratory tract, often caused by a respiratory viral infection; swelling of the mucosa of the eustachain tube progressing to obstruction the narrowed section, the isthmus, secretions that are constantly formed by the mucosa of the middle ear accumulate behind the obstruction and if a bacterial pathogen is present. AOM may result. The pathogenesis of fluid that persists for weeks to months after episodes of adequately treated AOM or persistent OME remains uncertain [1]. Recent studies have suggested that bacterial bio films on the middle ear mucosa may play a role in chronic otitis media with effusion or OME [11].

INFECTING MICRO-FLORA

AOM Microbiology

Streptococcus pneumomiae remains the most important bacterial cause of otitis media in most regions in the world. Relatively few serotypes are responsible for most disease, although there may be variation in serotypes in various regions of the world. The most common serotypes in order of decreasing frequencies are, 19, 23, 6, 3, and 18 [12,13] *Pneumococcal* vaccine(PCV7) introduce in 2000,contains serotypes 4,6B,9V,14,!8C,19F and 23F, which represents about 70% of serotypes responsible for acute otitis media [13].

H. influenzae is a common cause of otitis media, associated with non typeable strains in the vast majority of patients. In approximately 10% of cases; the otitis media is caused by *H. influenzae* type b and was frequently severe and accompanied by bacteremia or meningitis. Type b is now rare because of the efficacy of conjugate polysaccharide vaccine. Non type able strains of *H. influenzae* are significant cause of otitis media in patients of all ages [3]. *H. influenzae* is the primary pathogen in the unique conjunctivitis-acute otitis media syndrome [14].

Moraxilla catarrhalis has been isolated from approximately 10% of children with OAM and is usually associated with a mild form of disease. Before 1970, almost all strains of *M.catarrhalis* were sensitive to penicillin. Today, most strains produce β-lactamase and are more resistant to penicillin G, ampicillin and amoxicillin [15].

Staphylococcus aureus, Including methicillin and multidrug-resistant strains, is an uncommon cause of AOM but may be associated with persistent otorrhea that follows insertion of tympanostomy tubes [16].During the preantibiotic era, AOM caused by group A *Streptococcus* (GAS) was a frequent cause of severe AOM, frequently complicated by

mastoiditis and often associated with scarlet fever. For reasons unknown, AOM caused by GAS is now uncommon. A recent survey in Israel has identified GAS as being responsible for 3.1% of11, 311 episodes [17].

Two large scale studies in Israel and Finland have reported culture data from middle ear fluid obtained by tympanocentesis during AOM. Both studies reported *Streptococcus pneumoniae*, non-capusular *Haemophilus influenzae* (NCHi) and *Moraxella catarrhalis* as the most common causes of AOM [18,19].For Australian indigenous children, culture of ear discharge in cases of AOM with perforation (tympanocentesis has not been possible),found NCHi in 55 to 60% specimens, *S. pneumoniae* in 30 t0 40%,and *M. catarrhalis* in less than 10% of ear discharge specimens [20]. s Polymerase chain reaction (PCR) the mainstay of culture-independent methods, is increasingly used to test OM samples, because it provides greater sensitivity and can allow identification of bacteria in culture-negative samples.PCR is also useful in investigation of typical OM pathogens *Alloiococcus otitidis*,a controversial and difficult to culture proposed middle ear pathogen, which is commonly only detected by PCR[21].

Viral OM

Respiratory viruses have been isolated from the nasopharynx in up to 50% 0f children with AOM and have been detected in approximately 25% of middle ear fluids of children with AOM. Respiratory syncytial virus, influenza virus, entero viruses, corona viruses, andrhini virues were most common viruses found in the middle ear fluids [22]. Viral and bacterial infections are frequent and may be more severe than bacterial infections alone [23]. Chonmaitree and co-workers have noted that a higher proportion of patients with virus and bacteria in middle year fluids fail to clear bacteria 2 to 4 days after initiation of therapy compared with the group who had bacteria alone[24]

Miscellaneous OM Pathogens

Mycoplasma pneumonia was responsible for hemorrhagic bullous myringitis in a study of nonimmune volunteers inoculated with the organism [25]. However, the middle ear fluid of large number of patients (771) has been studied, and *M. pneumoniae* was isolated in only 1 case [26]. Although mycoplasmas do not appear to play a significant role in AOM, more patients with lower respiratory disease caused by *M. pneumoniae* may have concomitant otitis media [1]. Chlamydia trachomatis is associated with acute respiratory infections in infants younger than 6 months and is a cause of acute infection of middle ear in this age group. The organism has been isolated from middle year fluid of infants with acute infection [27].

Novel OM Infections

Uncommon forms of otitis include diphtheritic otitis, tuberculous otitis, otogenous tetanus, otitis caused by *Mycobacterium chelonae*, and otitis caused by *Ascaris lumbericoides* or Wegener's granulomatosis. Fungi are frequently associated with external otitis but rarely cause AOM; *Candida* and *Aspergillus* spp, have been isolated from middle ear fluids of immunod eficient patients who develop chronic suppurative otitis media [28]

CLINICAL MANIFESTATIONS

Acute Otitis Media can be classified as AOM or otitis media with effusion. The natural history of approximately treated AOM includes persistent middle ear effusion for several weeks in most children. AOM is fluid in the middle year in association with signs and symptoms of otalgia or otorrhea usually with fever [29]. A middle year effusion is virtually always present, except in the rare circumstances when practitioner may observe signs of acute inflammation in the hours

before fluid accumulates in the middle year. Pneumatic otoscopy is used to assess position, color, translucency, and mobility of tympanic membrane [29]. Local signs such as otorrhea with evidence of middle ear origin, bulging tympanic membrane is distinctly red, or local year pain should be sought. Fever is presumably indicative of AOM when there are associated local signs; in the absence of these local signs, fever often may be unrelated to middle ear effusion. Nonspecific signs and symptoms that do not help make the diagnosis of AOM include rhinorrhea, cough, irritability, anorexia headache, vomiting, or diarrhea. Physical examination (PE) in otitis media with effusion. Fluid in the middle ear in the absence of signs and symptoms of acute infection. Diagnosis of AOM by myringotomy is carried out by incision of the tympanic membrane. That or typanocentesis leads to recovery of the organisms [31, Ap.28]. On physical findings, both redness and bulging should be present. Merely immobility is not sufficient to make the diagnosis because this can be present in secretary otitis media [30]. Bacteria are isolated from 50% to 60% of cases and include *S.pneumoniae* (25%-50%), *Haemophilus influenza*(most cannot, be typed)(15-30%), *Moraxlella catarrhalis* (most are β lactamase positive) (3%-to 20%). Viruses also have also been isolated in pure culture, including respiratory syncytial virus (RSV), rhinovirus, parainfluenza, and influenza. *Mycoplasma pneumonaiae* is a consideration is a consideration and has been isolated with bullous myringitis.[29,30,31].

CLINICAL COURSE

Fluid persists in the middle ear for prolonged periods after the onset of acute otitis media, even though symptoms usually resolve within a few days after the initiation of antimicrobial therapy. About 70% of children with otitis media have fluid in the middle ear 2 weeks after the onset of the disease, 40% will have fluid 1 month after the onset, and 10% still have fluid 3 months after the first signs of middle ear infection [32].Patients with middle year effusion suffer from hearing loss of variable severity. On average, a patient with fluid in the middle year has a 25-dB(pure-tone average) loss [33]. Because the development of speech, language, and cognitive skills is dynamic during infancy when the incidence of acute otitis media is highest, there is concern that any impediment to reception or interpretation of auditory stimuli might have an adverse effect. Children with histories of recurrent episodes of acute otitis media score lower in tests of speech language, and cognitive abilities than their disease free peers [34, 35].

The results of microbiologic studies of middle effusions in patients with acute otitis media are so consistent that the choice of antimicrobial agents may be based on knowledge of the bacteriologic characteristics of otitis media acquired from other sites such as the throat or nasopharynx [1]. If the patient is toxic or has focal infection elsewhere, cultures of samples of the blood and the focal infection are warranted. Needle aspiration of the middle ear effusion (trypanocentesis) to define the microbiologic characteristics of the infection should be considered in select patients [1]

THERAPY AND PREVENTION

The antimicrobial agent of choice must be active against *S. pneuminiae, H. influenzae*, and *M. catarrhalis. Group A streptococci* and *S.aureus* are infrequent causes of OM. Gram negative enteric bacteria and methicillin resistant *S. aureus* must be considered when OM occurs in the new born infant [1]. Graig and Andes have examined the relationship between bacteriologic cure in otitis media and serum and middle ear fluid concentrations for various antimicrobial agents. They found that a bacteriologic cure required the presence of serum concentrations above minimal inhibitory concentration for at least 70% of the dosing interval [36] Amoxicillin remain the drug of choice for treatment of OM. The recent recommendation of doubling the dosage of amoxicillin to 80 mg/kg/day will achieve higher concentrations in middle ear

fluid and further reduce the number of children in whom amoxicillin therapy will fail because of resistant pneumococci [37]. Alternatives to amoxicillin include amoxicillin-clavulanate, three sulfa-or trimethoprim-containing preparations (erythromycin plus sulfisoxazole, trimethoprim-sulfame thoxazole), two crolides (azithromycin, clarithromycin), ninecephalosprorins (cephalexin, cefaclor, cefixime, ceftibuten, cefprozil, cefpoxime, cefuroxime, axetil, cefdinir), and one parenteral cephalosporin (ceftriaxone). Two topical fluoroquinilones, ofloxacine, and ciprofloxacine-dexamethasone otic, are effective in children who have typanostomoy tubes and suffer acute otorrhea [37].

Some children with AOM caused by bacterial pathogens improve without the use of antimicrobial agents [38]. Howie and Ploussard performed dual aspirates of middle year fluid in children with AOM 2 to 7 days apart, with placebo given instead of antimicrobial drug. They found that 19% infected fluids infected with pneumococci and 48% infected with *H. influenzae* became sterile. This discrepancy between the proportion of infections sterilized with two bacterial species indicates that a simple mechanical effect was unlikely to be responsible for microbiologic effect.

It is more likely that a host mechanism, probably based on humoral or cellular immunity, acts preferentially to rid the infected ear of *H. influenzae* more frequently than *S. pneumoniae[39*]. Jack F, *et al*. (1990) have examined 3660 children divided into three age groups 0-12 months,13-30 months and ≥31 months in a multi-national study, concluded that doctors certainty of diagnosis of AOM was linked to patient's age. Improved criteria or techniques for diagnosing AOM, especially in very young children, need to be developed.

Antibiotic treatment did not improve the rate of recovery of patients in this study [40]. Nasal and oral decongestants administered alone or in combination are used extensively for treatment of OM with effusion. The results of clinical trials, however have indicated no significant evidence of efficacy of any of these preparations, used alone or in combination, for the relief of signs of disease or a decrease in the time spent with middle ear effusion [41,Id,59].

Prevention of severe and recurrent episodes of acute otitis media includes chemoprophylaxis, use of bacterial and viral vaccines and surgery [1]

CONCLUSIONS

Acute otitis mediaanacute illness common in infants and children. Amoxicillin remain the drug of choice in OM. In AOM amoxicillin therapy in high doses is ineffective inbeta-lactamase producing pathogens

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